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EDITORIAL

THE SOCIAL ASPECT OF MEDICINE.

One aspect of the practice of medicine which is not stressed particularly to the medical student, but which is most important from the human side of medicine, is what we might term the social involvement of medicine. Perhaps an example will serve to clarify what we mean by this.

Suppose the following case, which is not a very remote possibility. Suppose an active young man, whose heart showed extrasystoles, which at times became very numerous, was seen by a physician who mistook these irregularities for auricular fibrillation; such a mistake is not impossible, for we have heard of that happening Now this young man is condemned to a state of semi-invalidism or complete invalidism unless he availed himself of the services of a competent cardiologist, with adequate diagnostic facilities.

We recognize the difficulties of making such a diagnosis, but what impresses us even more is the far-reaching affect of this diagnosis upon the individual's life. He would be changed from an active man, engaging in normal sports and activities, to a person who would have to lead a most restricted life, not being able to enter into the activities which any normal person enjoys; and, worst of all, he would probably assume that psychopathic outlook on life which many young invalids possess, because of the fact that he would not experience any discomfort or disability, and yet would be more or less forced to be a "looker-on."

In our clinics and ward-work we see patients who are suffering from this disease and that disease; we are interested in the clinical and laboratory picture they represent, and rightly so, for that is the prime purpose of our education. However, it is well to bear in mind that we as medical men have a very serious responsibility in this regard. We should adopt the attitude that we will not condemn a man or woman to a radical change in their social life unless we have made absolutely sure of our diagnosis, having availed ourselves of every possible advanced means of diagnosis if necessary.

THE QUALITIES OF A DOCTOR.

According to Dean B. C. H. Harvey of the Chicago Medical School, the three main qualifications necessary to a doctor can be represented by three S's.

The first is sympathy — upon which, as Osler said, medicine is founded. Sympathy was the first quality primitive "doctors" knew, and still is the mainstay of all physicians, the one quality which is effective when all other measures fail.

With sympathy alone, however, we cannot cure disease; thus to the rescue of the patient comes the second and more important agent — science. It is the duty of the real physician to know science and to bring its knowledge to the door of the patient, as it is also a crime to neglect the precepts of science or to be ignorant of them. "Most people would prefer to be cured by science without sympathy than to be followed by a funeral procession with a sympathetic ignorant doctor in the leading place."

However, even with all the sympathy in the world, and with all the knowledge of science known to man, a physician is no better than anyone else. He must know how to apply his knowledge; he must be able to observe carefully, palpate intelligently, auscultate with an understanding ear, and be able to interpret laboratory findings in their proper light. In short—he must have skill.

"Sympathy, science, skill — they all sum up in service. That is the glory of medicine. The obligation to serve is its religion. Need makes of it the supreme appeal. Above all else, the true doctor heeds its call."

THE DIPLOMATE.

The Journal has been honoured again by having one of its last year's articles reprinted by "The Diplomate" —the second such article to be reprinted from this Journal. Dr. Hodgson's "Notes on Investments" appeared in the January, 1933, number of "The Diplomate." This magazine is published by the National Board of Examiners of the United States. The publication deals with the activities of the National Board and also publishes articles of general interest to medical men, most of which are reprints. It is, indeed, an honour for us to have this our second article reprinted in such a publication.

INFECTION OF THE NOSE AND THROAT

WITH COMMENTS ON SOME OF THE SEQUELAE IN THE LOWER RESPIRATORY APPARATUS

By HARRIS McPHEDRAN, M.B. (TOR.), F.R.C.P. (C).

If we could keep pure the air, water and food that go into the body through the nose and mouth, what a multitude of diseases would be avoided. The common cold in the head is still treated with scant respect by the most of us who are, however, alarmed by the red placard of Scarlet Fever, or the yellow one of Diphtheria. And yet if the morbidity and mortality following in the wake of the former were duly considered, we should find a trail of diseases and disasters that would make us shudder.

The acute antrum, mastoid, frontal sinus, with in turn their complications, arthritis, sinus thrombosis and brain abscesses, follow this "cold in the head," as also do bronchitis, bronchopneumonia, bronchiectasis and pleurisy. Sydenham is reported to have said that more people die of colds than of pestilence

What is the cause of these colds? From time immemorial they have been attributed to "sitting in a draught," "getting the feet wet," "getting chilled." These are all factors, but surely not the only ones, as demonstrated by the conditions under which the men lived in the trenches in the Great War, and yet they were comparatively free from colds

Smiley[1] finds upon investigation that:

(1) There is a definite reciprocal relationship between the incidence of acute respiratory infections and the mean outside atmospheric temperature.

(2) That there is apparent a definite reciprocal relationship between the incidence of acute respiratory infections and the average daily hours of sunshine.

(3) That the peak months for acute respiratory infections year after year were December, January, February and March, with their variable temperatures and high winds laden with dust, dirt, and in cities, gas.

There is another factor to which enough attention is not paid, and that is the general physical condition, and particularly that of the nervous system. General exhaustion from overwork or worry is one of the most potent predisposing factors; and so we see colds develop in those who for one reason or another are tired out, or in those temporarily debilitated, e.g., growing girls at the time of menstrual period. There is under observation one such case at the present time, where month after month during the winter the patient develops a severe nasopharyngitis that keeps her in bed a week to ten days; and this condition develops in spite of removal of foci of infection, tonsils, adenoids, etc. Leonard Hill[2] has shown that the person with a turgid, dry mucous membrane in the nose and throat, the result of being in a warm, stuffy room, is more susceptible to infection than the one with brisk circulation in these membranes when out of doors, even in cold weather, and proves in brief that "to keep your feet warm and head cool" is scientifically sound in the prevention of colds. Given some combination of these untoward conditions in an individual, infections all too frequently occur.

Shibley, Hanger and Dochez[3] made observations of the normal bacterial

flora of the nose and throat with the variations occurring during common colds, and reached the following conclusions: That (1) the normal basic flora of the nose included principally staphylococcus albus, diphtheroids; (2) the normal basic flora of the throat includes principally Gram-negative cocci and non-haemolytic streptococci, B. influenza and diphtheroids; (3) no bacteria were found in early cold cultures to which a causative role could be assigned; (4) in the course of colds the basic flora of the nose was often scanty in the early stages and the throat showed reduction of the basic flora; (5) certain organisms were prominent in colds usually as late or secondary invaders, staphylococcus aureus, streptococcus haemolyticus and B. influenza, and there was a striking increase in incidence of streptococcus haemolyticus in throat infections.

A great deal of work has been done on colds in the head. Kruse[4] and Foster[5] reported the successful transmission of colds by inoculation of healthy individuals with nasal washings obtained from those suffering from colds and passed through Berkefeld fillers. Many others have confirmed these experiments.

In all too many instances the secondary invaders are the organisms that cause the most of the trouble, and so in the wake of a cold in the head we have the upper respiratory tract diseases, sinusitis (antral and frontal), otitis media, mastoiditis, and the lower respiratory tract diseases, bronchitis (acute and chronic), bronchopneumonia, bronchiectasis, pleurisy with effusion and bronchial asthma.

There are some features of these diseases that I would like to speak of briefly.

Bronchopneumonia, Lord says, "has its origin almost constantly in bronchial catarrah." This latter arises only too frequently from an acute descending infection of the respiratory tract. It is the menace constantly to be kept in mind in any cold in the head or throat or trachea, and is the condition particularly in the young, the aged and the debilitated that should prompt us as physicians to treat all colds seriously and insist that victims of this disease should be treated as sick people, be isolated in bed and kept there till the disease has subsided. This is a matter of education. The writer has seen an acute nose and throat infection disappear entirely three days from the inception of the disease, if the patient stayed in bed, and on the other hand hang on ten days to three weeks if he or she insisted, as most do, in attending to the ordinary daily duties—a menace to his own health and that of others.

This is the disease that is the nightmare of the surgeon. I should like to urge with all my powers of persuasion and emphasis of well-known facts which he who runs may read, that none of our patients who can be carried over to the warm days of the year be operated on in the winter months. This is especially applicable if the operation involves manipulation of the upper abdominal viscera, e.g., in cholecystectomy under local anaesthesia. Therefore, not knowing when it may come and who may be the victim, let us play safe in the best interests of the patient. Further, no patient, unless under very exceptional circumstances, who has an acute infection of the nose, throat, trachea, bronchi, should have any operation till the infection has entirely disappeared—a matter of usually about one month.

I recall all too vividly such a case. A patient, male, in the forties, came in the fall of the year to the city for cholecystectomy. He was found on examination to have an acute bronchitis. Operation was delayed some two weeks, during which time he was under appropriate treatment in hospital. At the end of this time the throat appeared normal and the lungs were clear of rales. He was anxious to go home and operation was undertaken and successfully done, only to have him die in a

few days of bronchopneumonia. Despite his request for operation and his apparent recovery from the acute infection, he should have been sent home and advised not to return for operation till the warmer days had come.

Chronic Bronchitis. Some writers claim that this disease seldom develops from the acute form. I am inclined to this view from my own experience because those having the acute form stay in bed till the disease subsides. Where the chronic disease obtains one finds almost invariably a history of discharging nose or repeated sore throat, evidence of chronic disease in antra sinuses or tonsils. The patient is not actually ill and these causes run on for weeks, especially in children, before any advice is sought. On examination they show coarse bubbling and wheezing rales, particularly over the bases of the lungs posteriorly, with, it may be, little constitutional disturbance beyond that produced by incessant coughing. The focus of infection is found in diseased antra, sinuses, tonsils, and successful treatment depends primarily on eradication of such foci of infection. Only too frequently there develops in cases of this kind bronchiectasis, a condition much more frequent than is generally considered.

A patient, male, age 50, consulted the writer, complaining of constant cough and expectoration. He stated he had taken ill six weeks previous to his examination, with a cold in the head, sore throat and soreness behind the breast bone. The cough became persistent, and as the days went on expectoration became more profuse till at the time of observation he was bringing up four ounces of mucopurulent sputum in twenty-four hours. He had a bronchitis of both lower lobes, worse on the left side, where there were not only coarse bubbling rales, but distinct bronchial breathing with a hint of the cavernous element in it. He had not only a chronic bronchitis, but also, I believe, a bronchiectasis, and as a focus of infection, badly diseased tonsils.

Improvement and recovery in cases not too advanced, takes place in these patients, if they are kept in bed and other such measures such as the removal of foci, control of cough, postural drainage, are instituted, but they should not be out of bed till the *lungs are clear* of rales. Many of us, I believe, are misled by the disappearance or marked lessening of the cough during the summer, but in spite of diminution or disappearance of symptoms in child or adult, in summer or winter, rest in bed should be insisted on till all rales have disappeared and thereafter for a considerable time as little work as possible should be thrown on the lungs. Moreover, these patients should be warned when colds in the head are contracted in the future to immediately seek their beds and stay there till the infection has subsided.

Asthma and bronchitis of varying degree not infrequently follow in the wake of repeated head colds, and relief will only be obtained by removal of polypi, nasal or antral, drainage of infected antra, frontal sinuses or the removal of diseased tonsils. Two cases recently have impressed this latter procedure on me.

One patient was a man in the thirties, whose life had become wretched through attacks of asthma coming on each night shortly after retiring. The tonsils were found badly diseased and tonsillectomy has so far given complete relief.

The other patient was a man in the sixties, whose attacks of asthma followed an acute bronchial infection, probably broncho-pneumonia, early in the winter of 1926. Breathing through the day was somewhat difficult, but his nights were terrible. The tonsils were found badly diseased and were removed, with great relief of all signs and symptoms; so much so that after eighteen months of chronic invalidism he is now back at his desk. Just here I would like to bear testimony to the efficacy of Ephedrine Hydrochloride,

the dose ¾ grain or more, in giving relief from the asthmatic attacks at night. The drug is taken by mouth and in about half an hour affords the sufferer relief from the spasm and carries him in comfort through the night. Its action is similar to that of Adrenalin in that it inhibits spasm of the bronchial muscle, but it has this advantage over Adrenalin that it can be taken by mouth, and one dose usually suffices to procure a night's sleep. One patient recently told me that while the attack of asthma was relieved, sleeplessness was produced and he refused to take the drug. Another patient who had taken it nightly for about three weeks developed most distressing cramps in the thigh and calf muscles, but these symptoms entirely disappeared as soon as the drug was discontinued

Acute Serofibrinous Pleurisy. This is considered tuberculous in the majority of cases, but there is a definite non-tuberculous pleuritis. I was taught, as were many of you, that a primary pleurisy with an effusion was tuberculosis in 90% of the cases Most of us, I am sure, feel now that percentage is too high. Lord[6] got positive results for tuberculosis in 22.7 per cent. of his cases by animal inoculation. He quotes Le Damamy as obtaining positive results in 85% of 55 primary cases by the injection of 10 - 50 cc. and as much as 300 c.c. of fluid, and Musgrave as obtaining positive results in 54.9% of cases of pleural effusion examined by animal inoculation, etc. So many cases of clear sterile effusion were seen during the flu epidemic in 1918-1919 that the writer became convinced that they certainly were not all tuberculous, and has set it down as a clinical guide that where an effusion is preceded by an upper respiratory tract infection, it is likely non-tuberculous. However, as such a large per centage of pleurisies with effusion are known to be tuberculosis, one should consider them such till the contrary is proved by history, physical examination, animal inoculation and X-Ray.

Do not let us forget in these sterile pleurisies with effusion, non-tuberculous by inoculation and following in the wake of a sore throat in young people, the possibility of their being a manifestation of rheumatic fever.

A Word As to the Physical Signs:

Large effusions are readily diagnosed. Smaller effusions half way up to, or even up to the angle of the scapula, are not infrequently overlooked. There are several reasons for this, the most important being that the back of the chest is not inspected in "good light" and the movement of each side of the chest watched.

Secondly, that percussion is not carefully done. Light percussion should be used and an earnest endeavor made to outline the resonant area of the chest without regard to the given anatomical position of the lungs or heart.

Thirdly, no trouble being taken to determine the expansion of the base of the lung.

Fourthly, not realizing that with the smaller effusion, e.g., up to the angle of the scapula and around in a curved direction to the anterior axillary line, the breath sounds are bronchial and rales not infrequently present, and that towards the upper limit of the non-resonant area the voice sounds have a nasal twang which if heard is pathognomonic of effusion.

A word in conclusion as to the treatment of these effusions. In my experience, the great majority get better if the patient is kept in bed on restricted fluids with moderate purgation. Only occasionally is paracentesis of the chest necessary, except for diagnotic purposes, and when done usually the removal of a small amount is sufficient to start absorption and to relieve any distress. Rapid removal

of large amounts of fluid is a bad practice, especially if the lung has been collapsed for a considerable time. I have seen great and unnecessary distress caused by this procedure.

These are some of the conditions that follow in the wake of so-called colds in the head, and the purpose of this paper will have been fulfilled if it arouses a new interest and necessary action in these infections with their high morbidity and not infrequently, mortality.

References:

1. Smiley. Amer. Journal Hygiene. Vol. 6, 1926.
2. Leonard Hill. B.M.J. 1916, Vol. 1, p. 541.
3. Shibley, Hanger and Douchez. Journal Exper. Med. p. 415, 1926.
4. Kruse, Munish Med. Journal, p. 1597, 1914.
5. Foster, J.A.M.A. Vol. 66, p. 1180, 1916.
   Foster, Journal Infectious Diseases, Vol. 21, p. 451, 1917.
6. Osler's and McCrae's System of Modern Medicine.

THE USE OF ENDOCRINE PREPARATIONS IN SEXUAL DYSFUNCTIONS

By W. G. COSBIE, M.C., M.B.
Department of Obstetrics and Gynaecology.

The whole question of pelvic physiology has been re-conceived in the last twenty-five years. To review the experimental work of a host of investigators is to lose oneself in its magnitude and to be overawed by the persistence and ingenuity of their work, which has laid the foundation of our present knowledge.

Since the work of Hitchman and Adler was published in 1908, it has been recognized that endometritis of infectious origin is very rare, and that the hyperplastic changes in the endometrium, far from being pathologic, are generally the normal changes of the menstrual cycle. At the same time, other investigators began the elucidation of the cyclic changes in the ovary and soon a correlation of the two became manifest It is only in the last ten years that the endocrine chain has become extended to include the pituitary gland, and that the interminable interweaving of other glands of internal secretion and their bearing on this more and more complex picture has come to be recognized.

Unless we base our conception of any sexual dysfunction on the basis of a known physiology, our treatment is apt to be sadly in error. Novack has said that it would be most unfortunate if the eager clinician should apply half-proved theories or speculative hypotheses to his special problems. The commercialization of endocrine preparations lends itself to this, and the whole structure is in danger of collapse from unwarranted exploitation. Let us, therefore, review our present knowledge and see on what foundation we can establish a rational therapy.

It is held that the ovary manufactures two hormones. The first, developed in the Graafian follicle, is a growth hormone and prompts the growth and increased vascularity of the uterus. It is responsible for the proliferative phase of the endometrial cycle. The peak of the production has been proven to coincide with ovulation, which is marked by the occurrence of oestrus or heat or rut in lower forms of life. For this reason it is known as oestrin. Frank named it folliculin when he first

determined its presence in the Graafian follicle, and Doisy, who first reduced it to its crystalline form, coined for it the name theelin.

The second hormone developed by the ovary comes from the active corpus luteum and is called progestin. It prompts the secretory phase of the endometrium — the pregravid phase — and, in the case of pregnancy, the formation of the decidua, and controls the nidation of the fertilized ovum. These two hormones are to a degree synergistic in that oestrin prepares the endometrium for the action of progestin; on the other hand, they are antagonistic, as oestrin stimulates whilst progestin soothes the uterus.

If pregnancy ensues, a new source of hormone production develops which acts through the pituitary gland and prolongs the life of the corpus luteum, while should fertilization of the ovum not occur, the corpus luteum regresses, the pregravid endometrium is cast off, and menstruation comes on.

The pituitary gland is made up of three component parts, the anterior, intermediate and posterior. The former provides the hormones which activate the ovary, prompts its function during adolescence, and maintains it from puberty to the menopause. Not only does it do this, but it also produces hormones which influence body growth and general metabolism. There are two anterior pituitary sex hormones named by Zondeck, Prolan A which develops the follicle and ripens the ovum, and Prolan B, which causes luteinization of the mature follicle and so the development of the corpus luteum. It is evident, therefore, that as the ovary controls uterine function, so the anterior lobe of the pituitary controls the ovary. The Pars Intermedia probably prepares the secretion, which is stored in the posterior lobe and is so well known to all of us, namely, pituitrin. Recently this substance has been shown to be composed of two separate hormones—oxytocin, which has the property of stimulating uterine muscle to contract, and vasopressin, which effects smooth muscle fibres elsewhere in the body and raises the blood pressure and stimulates peristalsis.

No consideration of these glands of internal secretion would be complete without referring to the thyroid. The inter-relationship is manifest by the enlargement of the gland noted during pregnancy and menstruation. The thyroid is the universal activator. Its dysfunction profoundly affects the whole gamut of sexual activity.

Now, due to the work of Collip, the placenta has assumed the role of an additional gland of internal secretion. From it he has extracted three hormones (1) oestrin, (2) emmenin, an oestrogenic hormone, biologically and chemically different from oestrin; and (3) anterior pituitary-like hormone (A.P.L.).

According to Collip, the interrelationship between ovary, pituitary and placenta is as follows: The pituitary is the master gland and is entirely responsible for the maintenance of the normal cyclic activity of the ovaries. During the course of each cycle the ovaries influence by their hormones the accessary genital tract. In the case of the human subject, this influence is most clearly manifested by the uterus, the endometrium of which undergoes a series of changes which are intimately related to the phenomenon of menstruation.

When impregnation and implantation of an ovum occurs, the ovarian cycle ceases, to all outward appearances at least, for the duration of pregnancy. During this period, first the decidua and later the placenta flood the system with the anterior pituitary-like principle. In the early weeks practically no oestrin or emmenin is produced by the placenta, but during the later months all three hormones are liberated in large amount. The pituitary gland has been shown to be less active in its gonad stimulating power during pregnancy.

A Modern Conception Of Menstruation

The application of these physiological facts to the primal sexual function of menstruation appears to be clear and concise. But this is not so. Quite recently Hartman working with monkeys, which menstruate as do humans, demonstrated that menstruation does occur without ovulation. He proved that this phenomenon was due to an anterior pituitary hormone working independently of the ovary, and clinical observation has since determined that this also occurs occasionally in women. We must recognize, therefore, two types of menstruation, one preceded by ovulation and luteinization, and the other not. Clinically, this second type of menstruation, sometimes passing on to menorrhagia, occurs at either end of the active sexual life. Consider also this fact as related to the question of sterility and the treatment of amenorrhoea. In the words of Hartman, there is a "low threshold bleeding," that is, bleeding occurs in the non-ovulating woman more readily than ovulation and the pregravid changes.

A Modern Conception Of Parturition.

We have all wondered what it is that determines the onset of labour. Why is it that a medical induction works or fails apparently under identically similar conditions? Or, again, what is the modus operandi of habitual abortion? Without going into substantiating arguments, I quote from Smith and Watkins: "Just before delivery the outstanding endocrine situation is this: folliculin has reached its highest level, the luteinizing hormone has decreased, and the corpus luteum has apparently become insignificant. The effect of progestin or the luteinizing hormone is known to inhibit the birth mechanism. A synergestic effect of folliculin and the oxytocic principle of the posterior pituitary in stimulating uterine contractions has been demonstrated by numerous investigators."

Clinical evidence substantiates these findings. Parturition normally occurs when menstruation would ordinarily have been expected. Also, abortion is more particularly liable to occur at the menstrual time, especially in the early months.

The application of our knowledge relative to physiology is an important factor in the diagnosis and treatment of endocrine disorders of the reproductive system. Amenorrhoea, both primary and secondary, menorrhagia of adolescence, maturity and the menopause, sterility and abortion, dysmenorrhoea and the vasomotor disturban-

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ces of the climacteric are forms of disease in which hormone therapy seems particularly applicable.

Unfortunately, organotherapy has not kept pace with the progress of physiology. As Graves aptly remarks, therapeutic success has been so meagre that it would appear that the mountains have laboured and brought forth only a ridiculous mouse. I shall try to enumerate certain reasons for this discrepancy.

(1) The early preparations of ovarian and corpus luteum extracts, with which we are all so familiar, pluriglandular extracts and many proprietary remedies which included ovarian extract in their formulae, contained a very small amount of potent substance, and this suffered rapid destruction in the gastro-intestinal tract.

(2) It is recognized that in many cases in the past we have been treating the wrong gland. In the case of the thyroid, the estimation of the basal metabolic rate is indicative of the activity of the gland, but it is only very recently, indeed, that tests have been developed which indicate where the hypo-function lies in the female hormone system. In no type of disease is exhaustive investigation so necessary to determine the weak link in the chain.

(3) Experimental results in such small animals as the mouse, rat and rabbit, emphasize the need for tremendous doses of even the newer and more potent preparations, so that the actual administration becomes a real problem apart from the almost prohibitive expense which this entails. Naturally this is a point which the pharmaceutical houses, anxious to retail their wares, are not likely to emphasize.

The hormone preparations now available are those from the ovary, anterior pituitary and placenta. Folliculin, progynon and theelin are amongst the most potent ovarian preparations and the ones in commonest use. Collip's emmenin prepared from the placenta also comes under this heading, and has nearly the same therapeutic uses. Corner and Allen have isolated the hormone of the corpus luteum — progestin — but at present it is not available for therapy.

The preparations of anterior pituitary hormone at present available for use seem to be principally of the nature of Prolan B, that is, the luteinizing hormone. The source is either from the pregnant urine up to the fifth month of pregnancy, or Collip's preparation of A.P.L. extracted from the human placenta. Because of the expense of the standardized products, of which Prolan, Follutein and Antuitrin are the best known, Mazer and Goldstein have treated deficiency cases requiringanterior pituitary hormnoe by injecting whole pregnant urine, after detoxicating with aether and filtering through a Berkfeldt filter.

Clinical Application of Female Hormones.

Oestrin is used in amenorrhoea, oligomenorrhoea and hypomenorrhoea. Its effect is to combat the uterine hypoplasia, which is almost invariably present. It renders the uterus responsive to whatever ovarian function there may still be present. It is purely substitutive therapy. The hormone does not stimulate the ovaries themselves or the extragenital glands concerned with the menstrual function. Oral administration is satisfactory, as oestrin is not affected by digestion and it allows prolonged and constant administration. According to Mazer and Goldstein, the usual requirement is 1,200 rat units daily by mouth for a period of two or three months.

Many observers, including Graves and Novack, have reported on the favourable effect of oestrin in controlling the constitutional symptoms of the menopause. The hypersensitivity of the vegetative nervous system, which manifests itself in flushes, nausea, dizzy spells, headaches and general irritability, is attributed to lack of follicular hormone, and oestrin has been shown experimentally to have a controlling

effect. A dose ranging from 30 to 100 rat units orally, or 10 rat units hypodermically, given daily, is advised.

The prime influence of anterior pituitary sex hormone is on the ovaries. As the motor of the ovary, it promotes a proper ovarian cycle and is almost a specific in the treatment of functional uterine bleeding of puberty and maturity. The hormone which has been isolated is not entirely pure Prolan B, but almost so. Therefore, the effect is to prompt luteinization, and a mobilization of progestin which transforms the characteristic hyperplastic endometrium into a pregravid one. In those cases where immediate control of bleeding ensues, it is held that an already present but imperfect corpus luteum is stimulated to full development and function. The anterior pituitary hormone is destroyed by digestion, and therefore must be given hypodermically. Mazer and Goldstein advocate a large dose, 100 to 200 rat units daily, to control functional bleeding. They also use small doses, 2 to 4 rat units daily, in conjunction with oestrin, to correct amneorrhoea. They believe in this case that the effect is to stimulate the ovary as a whole, and claim that the small dose does not risk the untoward effect of rapid conversion of the follicle into a corpus luteum, which would delay menstruation.

With regard to menorrhagia at the climacteric—this common condition has been known by many ill-fitting names — fibrosis uteri, idiopathic uterine haemorrhage, chronic metritis, &c. It is now known to have a definite pathology developed as the result of age or concurrent disease. This is a fibrocystic condition of the ovary, resulting from numerous follicles never coming to full maturity. The prolonged, excessive secretion of oestrin results in chronic glandular hyperplasia with associated menorrhagia. Hormone therapy is unavailing, and radium and X-ray treatment is established as the cure par excellence.

As Canadians we are particularly interested in the work of Collip and his collaborators. As before stated, he has isolated an oestrogenic hormone, emmenin, which in its pure form measures up to the Prolan A of Zondeck. Ayerst and McKenna have prepared this under the trade name Emmenogen, and it is specific for amenorrhoea. The dose suggested is one teaspoonful three times a day.

A less pure preparation, Emmenodyne, which contains an appreciable amount of oestrin, is considered more effective in the treatment of dysmenorrhoea, migraine of ovarian disfunction, and the vasomotor disturbances of the natural menopause.

Collip's A.P.L. has met with considerable success in the treatment of menorrhagia and menopausal bleeding. It is advised to give 100 rat units on alternate days for five days, commencing ten or twelve days before the expected period. It is believed that this hormone is beneficial in the treatment of habitual abortion, due to its stimulating effect in maintaining a healthy corpus luteum. At the present time observations are being made along this line at the Toronto General Hospital.

SURGICAL TREATMENT OF ANGINA PECTORIS*

By ALEX. A. ROGOW, '33.

The surgical treatment of angina pectoris is based on the hypothesis that the stimuli which give rise to the symptom pain arise in the heart and are carried by some nervous pathway to the spinal nervous system, where these impulses overflow and stimulate the somatic sensory neurones supplying the upper thorax, arms and neck. The surgical act is aimed at the division of this narrow arc, thus preventing the patient from recognizing the symptom pain. As the pathological condition which causes angina pectoris is still unknown, there is no intention of eradicating the disease by surgery. It is a method of treatment which is purely symptomatic, and therefore identical in purpose with the division of the sensory root to the Gasserian ganglion in cases of trigeminal neuralgia.

To obtain relief from pain we must know, first, what causes the pain; and, second, over which fibres the afferent and efferent impulses are mediated.

The most widely approved theory of the cause of pain is that of anemia of the heart muscle, due to an inadequate coronary circulation, whether there is coronary sclerosis or an apparently normal heart. Angina pectoris is much more frequent when the coronaries are severely sclerosed than when they are healthy. The anginal attack arises from a disturbance of the balance between the work of the myocardium and its blood supply. Looked upon in this way, the theory can account for anginal attacks in perfectly healthy young adults, since even healthy coronaries can be faced by an excessive demand. The theory also explains the many cases of coronary disease without anginal symptoms. In these it may be assumed that the occlusion has occurred so slowly that sufficient anastomosis has had time to develop to maintain the balance. In the angina due to syphilitic aortitis, partial and sometimes complete occlusion of the orifices of the coronary arteries in the root of the aorta is responsible for the condition. The hypothesis of spasm of the coronary arteries causing angina pectoris is untenable.

To bring about the relief from pain a thorough knowledge of the anatomy and physiology of the nervous system of the heart and its vessels must be at hand. This will not be dealt with in this paper, but probably a brief review of the salient points of the nervous pathways to and from the heart would not be amiss at this point.

The heart is supplied by the sympathetic and the parasympathetic nervous systems. The sympathetic supply arises from the connector cells situated in the lateral horn of grey matter in the upper four or five thoracic segments. The connector or preganglionic fibres pass out in the anterior root corresponding to the segment from which they arise, and then enter the mixed spinal nerve. The connector fibre soon leaves the anterior division of the spiral nerve as the preganglionic fibre. The preganglionic fibres of the upper four or five thoracic sympathetic ganglia synapse with excitor cells in these ganglia and postganglionic fibres, go directly across to end in the plexuses supplying the heart In addition to these, preganglionic fibres traverse the sympathetic ganglia in the thorax and end in the cervical sympathetic ganglia by synapsing with the excitor cells there. From these cells postganglionic fibres go to the heart by way of the upper, middle and lower cardiac nerves. These nerves run through the neck into the thorax and join the cardiac plexuses.

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The parasympathetic supply is from the vagus nerve. The connector fibres arise from connector cells found in the dorsal nucleus of the vagus in the floor of the fourth ventricle. These fibres run through the neck as the superior and inferior cardiac branches, and end in the cardiac ganglia. The postganglionic fibres are distributed to the heart muscle.

The visceral afferent fibres arise in the heart and proceed directly without interruption via the middle and inferior cardiac nerves of the cervical ganggia and through the fibres running directly across from the heart to the cerebrospinal ganglia, and there synapse with a unipolar cell. The fibre then enters the spinal cord and synapses with the connector cell, thus completing the sympathetic reflex arc. The superior cardiac branch of the superior cervical ganglion is probably made up of efferent fibres only. The parasympathetic reflex arc is probably similar. The central control of the autonomic nervous system is probably situated in the hypothalamus.

With this understanding, we may proceed to a critical review of the surgery in relation to angina pectoris.

The operative treatment of this condition was first proposed by Francois Franck in 1899. However, it was not until 1916 that Jonnesco in France practised it. He removed the upper three cervical and first dorsal ganglia on both sides. This was not popular, because of the difficulties associated with the operation. In 1923 Coffey and Brown presented five cases in which they performed a superior cervical ganglionectomy with division of the superior cardiac nerve from this gangnon, and Ionesco and Enarchesco.
served to ameliorate the pain.

In 1926 Cutler and Fine, after reviewing the literature and on the basis of some of their own work, came to the conclusion that a single or bilateral extirpation of the superior cervical ganglion or of the whole chain, will frequently give temporary or partial relief or none, and stated that the knowledge of the sensory innervation of the heart was not complete. In the early part of 1927 Cutler gave a review of the known anatomy of the nervous system of the heart at that time. Up to that time they were not aware of the connection of the heart with the central nervous system by direct fibres from the upper five or six thoracic sympathetic ganglia. He states that except for the connection of the vagi with the CN.S. in the brain stem, the connections between the stellate ganglion and the spinal cord at the level of the first dorsal nerve represent the only proven connections between the heart and the C.N.S.

During 1927 Cannon did some work on the innervation of the cat's heart. When the hitherto recognized nerves reaching the cat's heart were severed, and all known hormones excluded from action, the heart, nevertheless, became capable of marked acceleration if the animal changed from a resting to an excited state. He presents details of the search for the unknown accelerating agent, and comes to the conclusion that accessory accelerating fibres from the upper thoracic ganglia below the stellates mediate the faster beat. When these were removed, in addition to the removal of the previously recognized agencies causing the heart to beat faster, the heart remained steady within approximately twelve beats in spite of vigorous activity.

About the same time, Ionesco and Enarchesco, in France, working on stillborn foetuses, described, for the first time in man, nerves coming from the thoracic chain of sympathetic ganglia, below the stellate of the fifth going to the heart. They were quite constant and well developed. The left heart was better provided than the right, some fibres from the right side going to the left heart. They attained the heart either directly, through the aortic plexus, or through the cervical cardiac nerves.

It has been observed, up to that

time, that the results of the operation of stellate ganglionectomy were poor, and these poor results can probably be explained by the observations of Cannon, and Ionesco and Enarchesco.

Danielopolu, in France, objects to the removal of the stellate ganglion on two scores. In the first place, he believes that it causes damage to the heart muscle; and, in the second place, because it removes vasodilator fibres to the heart. He states this to be the cause of the poor results seen in cases of stellate ganglionectomy. He attempts to suppress the pressor reflex which he thinks is the cause of the attack. The pressor reflex comes into play when there is a rise of pressure in the aorta. This causes a flow of afferent impulses up the depressor nerve to the vagus centre and efferent impulses come down the vagus, causing a reflex slowing of the heart, and a fall in blood pressure due to a vasodilatation of the splanchnic blood vessels. He also states that in several cases of death due to angina pectoris the myocardium at autopsy was in good condition, and that the patient would have lived a long time if he had not died of the attack. By prevention of the pressor reflex he thinks he prevents the attack and prolongs life.

The criticism to be levelled at this is that there is not a depressor nerve in man comparable to that in lower animals Danielopolu reports a series of 28 cases in which the operation of cervical sympathectomy, without interfering with the inferior cervical ganglion, and section of all the branches of the vagus nerve in the thorax, was done. He states that the pain disappeared completely or nearly completely from 1-5 years without deaths or complications

It seems to me that the whole idea of the pressor reflex with regard to angina pectoris is wrong. In the first place in order that the pressor reflex may come into effect there must be a rise in blood pressure in the aorta. But, in angina, there is no characteristic rise in blood pressure. In the second place the manner in which the pressor reflex might cause an anginal attack is inconceivable.

Leriche and Fontaine in 1928 published their views on the subject which practically coincides with those of Danielopolu, viz., suprastellate sympathectomy with section of the depressor nerve.

In the past few years the problem has been approached from a different angle. Attempts have been made to prevent the occurrence of the symptom pain by preventing the pain impulses from registering on the C.N.S. The exact pathways of the pain impulses are not known, but it is a fact that the pain when it does occur follows mainly the thoracic nerve distribution. Therefore it is believed that the sensory afferent pain impulses must come mainly or entirely over the sympathetic fibres to the C.N.S. and not via the vagus. Therefore if the communicant rami of the sympathetic nerves are cut or destroyed from D1-D7 segments no pain impulses would register on the dorsal root ganglia; there would be no irritation of dorsal root cells and no pain sensations in the thoracic nerves.

On this basis the latest practice has been to inject alcohol around the sympathetic ganglia and their communicant rami, thus preventing them from functioning In 1928 White reported the results of this treatment in five patients. Although he drew some conclusions from this series, I think the series too small to be of much value.

In 1929 Swetlow published a paper in which he reviewed very well the pathways for the sympathetic and vagal fibres to the heart. He stressed the fact that the cardiac nerves of the vagus and of the cervical ganglia inosculate very freely with each other in the neck and therefore no matter what pathway is obliterated in the neck, other paths exist for the mediation of the sensory afferent impulses to the C.N.S. He states that even if the

sympathetic cardiac nerves of both sides were removed and both vagi, if possible, impulses from heart and aorta would still pass into the spinal cord by rami communicantes through D1-D7 segments. Therefore, his object is to destroy the poorly myelinated afferent sensory fibres from the heart which are passing from the sympathetic cords to enter the dorsal root ganglia. With injection of alcohol into the dorsal root ganglia or the sympathetic fibres in the vicinity of the dorsal root ganglia an intense Wallerian degeneration ensues.

He presents clinical evidence concerning pathways of cardiac pain as ascertained by subjective radiation. The radiation of pain is related quite consistently to those areas of the body supplied by C8-D7 nerves. Pain over C1-C2 is rare, and over the trigeminal a curiosity according to Swetlow. A complaint of pain along the outside of the arm is so rare that its existence is denied by him. Anatomically and embryologically it is quite likely that no afferent sensory fibres enter C4-C7 nerves. Therefore from the clinical point of view we can say that the impulses which produce pain pass through the dorsal root ganglia which supply the dermatonic segments innervated by C8-D7. He also states that these segments become hyperirritable and hyperaesthetic and can actually be demonstrated by pin prick, heat and cold. In 22 cases Swetlow found these zones limited to segments supplied by nerves C8-D7. These zones are called "Head" zones.

Head and McKenzie advanced the theory that pain over the distribution of the fifth nerve could be explained by an irritation of the fifth nerve nucleus by stimuli coming up the vagus nerve from the heart and registering on the vagus nucleus and then passing to the fifth nerve nucleus.

Operations on the superior and middle cervical sympathetic ganglia and the vagus in the neck have given poor results with regard to relief from pain, and show that if pain impulses do pass through the superior and middle cervical ganglia and vagus they do so in a very minor degree.

Swetlow experimented with animals and showed by his experiments that pain discharges from the heart and aorta are not transported by the cervical sympathetic chain. Some observers witnessed an attack of angina pectoric during an operation. Injection of the superior and middle cervical ganglia gave no relief, but injection of the stellate ganglion immediately suppressed the pain.

Swetlow reports his results in 22 cases of angina pectoris treated by paravertebral injection of 95% alcohol. Eleven cases gave 90-100% relief; 7 gave 50-85% and 4 gave 0-50% relief. Alleviation of pain lasted several months

Since pain was relieved by destruc-

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tion of the irritated ganglia C8-D7, therefore the impulses of pain were intercepted before entering the spinal cord, and since only nerves found between C8-D7 were destroyed, therefore the pathway of pain is through the rami communucantes and dorsal root ganglia between C8-D7 spinal segments. Five of the 22 patients complained of severe pain along the nerves injected. In some the pain was sharp and paroxysmal; in others a dull ache. In all the pain finally disappeared. This pain is due to the chemical irritation of the alcohol inciting an alcoholic neuritis. No operative or post-operative deaths occurred even in severe cases.

In 1929 J. C. White reported a series of cases treated by paravertebral block with alcohol. All his patients were first carefully examined and given medical treatment, and only on whose who did not improve was operation attempted. He says that very few contra-indications to operation occur, the few being active sepsis in the body and advanced decomposition. The objection has been raised that prevention of the pain sensations removes the danger signal to the patient and allows the patient to overexert himself. White says that this is no contra-indication, because shortness of breath, peculiar sensations in the region of the heart without pain, or milder attacks on the right side have always given adequate warning.

His method is a preliminary test injection of 5 ccs. of 1% procaine-adrenalin solution, injected around the trunks of the upper thoracic nerves as they emerge from the intervertebral foramina and give off sympathetic rami. This in itself provides relief for 36 hours. However, as soon as the intercostal anaesthesia develops 5 ccs. of 95% alcohol are slowly injected. His results are similar to those of Swetlow. In the patients that are a good operative risk, in addition to the above, he removes the stellate ganglion to avoid the 25% chance of a poor result following the injection of alcohol. His operative mortality with alcohol injection is zero; with total cervical sympathectomy, 21%; with partial cervical sympathectomy, 7.5%.

In 1931 Yater and Trewhella, of Washington, reviewed the results of the surgical treatment of angina pectoris. They state that the relief of pain is important not only from the standpoint of the suffering of the patient, but the pain itself may actually be injurious to the organism. They were of the opinion that operation should be reserved for the more severe cases. They analyze 138 case reports in which all types of operation in the neck are performed.

126 cases of operation on cervical sympathetic ganglia and nerves.

Complete relief in ..	40%
Partial relief in	29%
No relief in	27%
Results not recorded in	4%

12 cases in which cardiac depressor nerve thought to be cut.

Complete relief in ..	41%
Partial relief in	25%
No relief in	25%

No record in one case.

Therefore, of all types, complete relief was obtained in 40.5%, partial relief in 27%, no relief in 26%.

The reason for the relief in the 40.5% of cases is not apparent, because in no case were all of the afferent nerves resected. During the period of observation 33 patients died, 8 during or within a few hours of the operation, 7 lived 2-14 days, 4 died in two weeks to a month, one died in one month to a year, and three lived one to three years. Immediate operative mortality was probably 6.5%; therefore, with complete relief in 40.5% and an operative mortality of only 6.5% the operative treatment of angina pectoris would seem to be a justifiable procedure, especially when the cases of immediate

mortality with syphilitic aortitis are eliminated. Then the operative mortality is only 1.8%. However, of the survivors of the operation, 31% had serious or disagreeable postoperative complications of the nature of pains, and paraesthesias of variable duration. One of the commonest types was pain on the side of the face, jaw, or neck, also brachial neuralgia and others. Horner's syndrome always occurred after the Ionnesco operation.

They state that it was impossible to determine whether operations had any effect upon the course of the disease, but that their impression is that the course of the disease is not materially affected.

They summarize as follows:

Case For Operative Treatment.

1. Complete relief of original pain in 40.5% of cases.
2. Partial relief of original pain in 20.7% of cases.
3. Low immediate operative mortality when cases associated with syphilitic aortitis are eliminated.

Case Against Operative Treatment.

1. None or only partial relief in 53% of cases.
2. Postoperative paraesthesias with new pains in 31%.
3. Effectiveness of amyl nitrate or nitroglycerine for individual attacks of pain certainly more than 40.5%.
4. Apparent absence of influence upon course of disease.

They conclude by saying that the knowledge of the anatomy and the physiology of the innervation of the heart and of the aorta is incomplete, and that operative treatment should be performed only in selected cases to study the anatomy and the physiology of the heart and aorta, which gives information impossible to obtain from dissection on cadavers or experiments on living animals.

To sum up, then, two methods of the surgical treatment of angina pectoris have been reviewed, viz., various operations on the nervous pathways and the ganglia, and paravertebral injection of alcohol. The former has been productive of poor results, and carries with it a definite mortality. The latter has given better results, but has caused the patients severe discomforts in the form of paraesthesias over the areas injected. In my opinion the first method, of operations in the neck, should be abandoned and the treatment of paravertebral injection of alcohol reserved for the cases whose lives are made miserable by the pain, which can be relieved in no other way.

I should like to conclude by saying that the further progress of this treatment lies in our obtaining a better knowledge of the anatomy and physiology of the innervation of the heart.

Bibliography.

1. Danielopolu—Presse Med., 1922, 30.
2. Cutler—J.A.M.A., 1926, 86.
3. Cannon—Amer. J. Physiol., 1927, 77.
4. Jonnesco and Enarchesco—Compte Rend. Soc. de Biol., 1927, 97.
5. Cutler—Amer. J. Med. Sc., 1927, 173.
6. Leriche—Amer. Heart Journ., 1928, iii.
7. White—J.A.M.A., 1928, 90.
8. Swetlow—Amer. J. Surg., 1929, 9.
9. Danielopolu—La Presse Med., Dec. 1930.
10. Danielopolu—Rev. Belge Sc. Med., 1931, 3.
11. Yater and Trewhella—Amer. J. Med. Sc., 1931, 182.
12. Cutler—Surg. Gyn. Ob., 1932, 54.

ACUTE PANCREATITIS*

By DOUGLAS TELFORD, B.A., (B.C.), '33.

Introduction.

Acute Pancreatitis is the result of nothing more nor less than tryptic digestion of pancreatic tissue and, as such, is more correctly named acute necrosis. Whether the disease be of the hemorrhagic, gangrenous or suppurative type it is essentially the same condition, varying only in degree of severity or stage of development. Chronic pancreatitis, on the other hand, cannot be included within this unity, so will, I fear, find little mention in this paper.

The apparently increasing frequency of acute pancreatic necrosis, the unsolved riddle of its etiology, the high index of incorrect diagnosis, the diversity of opinion regarding its treatment and, finally, the staggering mortality of at least fifty per cent., make it one of the most interesting of diseases

Incidence.

Acute pancreatic necrosis is not as rare as common opinion would suggest. At least four cases find their way to the Toronto General Hospital public wards each year. Reports show a slight preponderance in the male sex with an almost uniform distribution throughout the third to the sixth decades of life. The disease may occur, however, at the extremities of life.

Anatomy.

In so far as certain features of the anatomy of the pancreas and its ducts bears upon the pathological and clinical aspects of acute pancreatic necrosis, this subject deserves elaboration.

The pancreas is a "J" shaped structure composed of head, neck, body and tail. It is a member of MacCarthy's so-called gastro-duodens-hepatico-pancreatic system as such lies in close relationship to other members of this group. The stomach rests upon its anterior surface, the two organs being separated by the omental bursa. The duodenum loops about its head, grooving its borders and in some cases being surrounded by a band of pancreatic tissue. The common bile duct runs in a groove on the surface or through a canal in the substance of the organ. This relation offers an explanation of some of the cases of jaundice concurrent with pancreatic disease.

The anatomical relations of the duct of Wirsung, the main duct of the pancreas, to the common bile duct are important as having a strong bearing on the pathogenesis of pancreatic disease. These two ducts join as they pass through the duodenal wall to form the ampulla of Vater This is a cone-shaped structure opening at its apex on the duodenal papilla. The ampulla, varying in length from 3 to 11 mm., is so constructed that in a certain proportion of cases a gall stone or plug of mucus, lodged at its apex, can convert the two ducts, entering at its base, into a continuous channel. [1]Mann and Giordano carefully reviewed the anatomic relations of the common duct of Wirsung in 200 consecutive autopsies. They found that in less than 20% of cases would it be possible for obstruction at the ampulla to convert the two ducts into a continuous channel. [2]Opie, on the other hand, would place the figuse at 32%, while [3]Cameron and Noble say that in 66% of specimens removed at autopsy it is possible to divert fluid from the bile duct into the pancreatic duct by means of a selected gall-stone actually placed within the diverticulum of Vater

The lymphatics of the pancreas have received much attention. Mau-

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geret,[4] in 1908, first demonstrated the anastomosis of the efferent lymphatics of the pancreas with those of the gall-bladder. [5]Franke in 1911 verified these observations and found a node at the neck of the gall bladder which communicated with the lymphatic vessels of the pancreas. [6]Bartels pointed out that the lymphatics of the duodenum are also very closely related to those of the head of the pancreas and passes no intervening nodes. These observations have an important bearing on the etiology of acute pancreatic necrosis and will be referred to when we discuss that phase of the subject.

Physiology.

The physiology of the pancreas is fairly well understood. The gland has two secretions, an internal and an external. The former, insulin, is intimately related to carbohydrate metabolism, whereas the latter is a potent factor in the enteric digestion of carbohydrates, fats and proteins. The ferments involved in the digestive process are produced within the gland acini The stimuli acting upon the cells of the acini are both nervous and hormonal in type and, when the latter are due to a substance, secretin, which is absorbed from the duodenal mucosa during digestion.

The newly secreted pancreatic juice is not fully active. The pancreatic amylase, I admit, can digest starches and the lipase fats, but the protein fermust pass into the intestine before it assumes its full proteolytic powers. In the intestine the pro-enzyme of trypsin is activated by a substance called enterokinase. In a test tube bile salts alone will activate the pro-enzyme as will certain products of bacterial activity and protein autolysis. I mention these facts because, around the activation of the trypsin revolves the solution to the pathogenesis of acute pancreatic necrosis

The flow of the external secretion through the pancreatic duct varies greatly, depending upon the stage of digestion. The pressure, too, varies, but is at all times less than that maintained in the biliary channels. This pressure is dependent somewhat upon the sphincter of Oddi which relaxes during the passage of chyme through the duodendum. This periodic activity of the biliary and pancreatic systems and the temporary relaxation of the sphincter suggests an explanation of the frequent onset of acute pancreatitis following the taking of a heavy meal. So much for the physiology, now for its application.

Pathogenesis.

We pass now to a consideration of the pathogenesis of acute pancreatic necrosis. As this most interesting disease proves to be nothing more or less than the outcome of tryptic digestion of pancreatic proteins we are challenged to explain why a physiological process which normally takes place in the intestine can be initiated within the gland itself.

There are five possible routes by which the activating substance may gain access to the gland

(1) Bile, infected or not, may journey up the pancreatic duct. The action played by the bile salts in the production of acute pancreatic necrosis was first demonstrated by [7]Claude Bernard in 1855 He injected bile and sweet oil in the pancreatic duct and produced necrosis of the gland. [8]Flexner and others showed that the constituent of the bile causing the activation was the bile salts and that the nucleoprotein component of bile was not only inert, but was actually protective. [9]Archibald and his associates demonstrated by chemical studies that bile salts were greatly increased in infected bile. Further experimentation has shown that aseptic plugging of the duct will produce chronic pancreatitis; that the injection of certain virulent bacteria cause either chronic or subacute pancreatitis; that the injection of infected bile is apt to produce a very

acute pancreatitis which is primarily necrotic and finally that the [10]injection of duodenal contents containing enterokinase will produce a similar pancreatic necrosis with very rapid death.

Having then fairly well shown that bile with or without infection can produce hemorrhagic necrosis, it is necessary to bring forth evidence to prove that bile really can force the locks which guard the mouth of the pancreatic duct. Mann, investigating this process, found that bile passed into the pancreatic duct in most instances at a pressure of 500 mm. of water and that in every case bile passed into the duct at a pressure of 800 m.m. of water. This reversal of flow is of more than experimental interest when we recall that the normal pressure of 300 m.m. of water, maintained by the sphincter of Oddi, may rise to 500 or 600 m.m. of water under conditions of hyperirritability of the gut. [11]Archibald believes that a spastic contraction of the sphincter may explain the retrojection in cases in which the acid content of the duidenum is high, chronic alcoholism and peptic ulcer. Here, too, might be mentioned the increase in tone of the sphincter following cholecystectomy and the increase to 1000 m.m. of water accompanying vomiting or deep inspiration.

In addition to spasm of the sphincter of Oddi plugs of mucus, edema of the duodenal mucosa or the presence of a stone lodged in the ampulla of Vater may bring about the same result. The [12]classical example of this is to be found in Opie's famous case of acute pancreatic necrosis in which a gall stone exactly blocked the duodenal orifice of the ampulla in such a way as to convert the two ducts into a continuous channel. From these demonstrations we must not conclude too much since the anatomical arrangement permitting such a result is only present in a fraction of all cases. Before passing judgment on the plausibility of this method let us consider the other possibilities.

(2) Doudenal contents may pass the sphincter of Oddi and folds of mucous membrane guarding the mouth of the pancreatic duct, to gain access to the gland. That this method is a real possibility in some cases must be admitted in view of the following evidence. Several cases of acute pancreatic necrosis have been reported confined to an accessory lobe drained by a duct having no relation to the common bile duct. In addition cases are seen at autopsy in which the main duct of the pancreas opens upon the duodenal papilla independently of the common bile duct.

(3) Infection may travel by way of the lymphatics to the head of the pancreas. This theory on first consideration sounds quite plausible because of the anastomosis of the lymphatics of the gall bladder, duodenum and pancreas. In order to explain the passage of infection against the flow of lymph, however, proponents of this theory must presuppose a block in the nodes further down the stream and consequent reversal of the flow of lymph in an attempt to establish a collateral circulation. [13]Deaver would describe the usual sequence of events as follows: Cholecystitis, lymphangitis, lymphadenitis in the course of the cystic and common duct, peripancreatic lymphadenitis, pancreatic lymphangitis, pancreatitis. Clinical evidence of this is obtained in the frequent observation by surgeons of a chain of enlarged lymph glands in the course of the lymph paths between the two organs, the gall bladder and pancreas. Pathological investigation reveals a coincident occurrence of local hepatitis in the region of the gall bladder bed and chronic pancreatitis in that part of the pancreas most freely supplied with lymphatics.

In spite of this suggestive evidence of the lymphatic origin of acute pancreatic disease we are forced to conclude that infection by this route does not cause the acute disease, but does cause chronic pancreatitis, where, in-

deed, it is popularly acclaimed the path of election.

(4) Infection may reach the pancreas by way of the blood stream to cause the activation of trypsin. Acute infection by this method is rare, although the association of acute pancreatitis with epidemic parotitis is now well established. Its association also with certain infectious diseases as typhoid fever or influenza or with certain suppurative conditions as appendicitis and furunculosis is recognized.

(5) Because of direct continuity of tissue, infection may reach the pancreas. Examples of this are perforating gastric or duodenal ulcer and carcinoma of the stomach.

In summarizing our discussion of the pathogenesis of acute pancreatic necrosis, I would like to say that the most plausible cause of the tryptic digestion of the pancreas is the first presented, bile either infected or not, passes up the duct to activate the trypsin. It is to be remembered that, although this is likely the method of choice in the majority of instances, the possibility of enterokinase passing from the duodenum and infection gaining access to the gland by way of the blood stream, etc., must be admitted in some cases.

Morbid Anatomy.

[14]The original description of Fritz in his Middleton Goldsmith lecture published in 1889, on the pathological details of acute pancreatic necrosis has never been surpassed. The naked-eye appearance of the pancreas either in the hemorrhagic, gangrenous or suppurative stage presents a great variety of pictures. The gland is usually enlarged to two or three times its normal size, although at times it maintains its normal volume. According to the degree of hemorrhage present the surface shows irregular, yellow, red or almost black areas studded upon a dull white field. The haemorrhage may, however, be so severe that the whole organ assumes a bluish black appearance. The cross section shows a marble-like surface.

According to the stage of necrosis one may find the gland ultimately extruded as a slough in an abscess cavity or part of the gland may be softened, and shreddy fragments of sloughing tissue may separate. In certain cases whether or not bacteria complicate the picture, there is apt to develop an abscess containing broken down tissue and hemorrhagic fluid. Such abscesses tend to point and may appear in the lumbar region or break through into the bowel or peritoneal cavity.

The miscroscopic appearance is one of necrosis. The process, beginning in the lumen of the acini, attacks first the centre acinar cells and later progresses outwards to involve the stroma. Only when the stroma is reached do the accessory lesions of hemorrhage and fat necrosis, etc., take place. The evolution of the process studied histologically agrees well with the theory of the entrance of the noxious agent by way of the ducts.

Several peculiar features of the pathological picture deserve special consideration. Pancreatic necrosis, as we mentioned formerly, is the result of tryptic digestion of pancreatic tissue proteins.

Hemorrhage is secondary to necrosis and results from the erosion of the vessel walls by the proteolytic ferment.

The blood tinged serous exudate in the peritoneum is probably due to the effect of the ferments travelling along the subperitoneal lymphatics. This exudate is usually sterile and is quickly absorbed.

Fat necrosis is the most striking phenomenon and was first described by Balser. It is not always demonstrable, but is when present, practically pathognomanic of acute pancreatic necrosis. The areas of fat necrosis appear as rounded or oval areas studded upon peritoneum, omentum, mesentery and liver. These areas are very conspicuous on account of their opaque

white or yellowish color contrasting sharply with the translucent golden yellow of the fat in which they occur. Particularly in the neighborhood of the pancreas, where they are most numerous, the foci of necrosis may be large and confluent.

These lesions are caused by the pancreatic lipase digesting small areas of fat to produce glycerin and soaps. Just as the bile when its outflow is obstructed, is diverted to other parts of the body so the lipase when damned back upon the gland, finds its way to distant parts of the body. Areas of fat necrosis have been found in the mediastinum, pericardium and even periarticular tissues suggesting a lymphatic or blood stream distribution of the ferment. As we pass now from the pathology to the clinical aspects of the disease we must bear in mind the peculiar features of the former when trying to explain the problems of the latter.

Clinical Manifestations.

The disease occurs more frequently in males, and is encountered as a rule in middle or late life.

Predisposing conditions are obesity, alcoholism, disease of the gall bladder and ducts, trauma and localized or general infections.

Attention has already been called to the essential unity in the various pathological pictures of the disease. A like assertion may be made of its clinical manifestations. The clinical picture, however, may vary from that diagnosed acute indigestion to the dramatic picture of a full-blown case.

Pain is regarded as the most outstanding symptom of acute pancreatitis. It is the first to appear, and, according to Moynihan[15], is so severe that no other abdominal catastrophe can produce such unendurable agony. Strangely enough, it follows the taking of a heavy meal in about 50% of cases, especially if cholelithiasis is coincident. The pain occurs with greatest intensity in the epigastric region, and may radiate towards the left chest, into the left flank or between the shoulder blades. With the development of a blood-stained peritoneal exudate it may extend downwards over the abdomen, but is rarely severe in this region.

Collapse is an outstanding feature, but is not marked as long as the haemorrhagic exudate is confined to the capsule of the pancreas. When, on the other hand, the exudate appears in the general peritoneal cavity the collapse is very profound. The pulse becomes rapid and feeble and the blood pressure falls. The respirations are fast and shallow, and a condition of dyspnoea develops which is characteristic of the disease.

A peculiar slate blue cyanosis often accompanies the collapse. It is more or less confined to the upper part of the body, but does not appear in patches on the abdomen and extremities. This phenomenon is thought to be due to both the collapse and the toxin circulating in the blood.

Nausea and vomiting, present in most cases, may make the differential diagnosis from high intestinal obstruction difficult, especially if occurring early. Retching and hiccoughing frequently accompany the vomiting because of irritation of the diaphragm by the swollen pancreas.

Subnormal temperature is significant especially in the early stages, and in as much as the pancreatic lesion is not inflammatory but merely necrotic, the temperature and pulse are not above normal. If the toxaemia is profound both become sumnormal, and the pulse may later become very rapid. The temperature rises if peritonitis occurs, or when in two or three days the inflammatory reaction supervenes. If suppuration does ensue, there follows the ordinary signs of infection, continued fevers and chills.

Jaundice is present in less than half the cases. It is due either to cholelithiasis or pressure on the common duct by the head of the pancreas.

Inspection of the abdomen shows slight distension in the epigastrium.

Palpation detects rigidity and tenderness in the same region, which may become generalized as a result of the agonizing pain. The general board-like rigidity seen in perforated hollow viscus does not occur, however In some cases the rigidity may be so slight that a mass deep in the epigastrium may be demonstrated by gentle palpation.

Intestinal obstruction with meteorism of an adynamic nature is often so prominent a feature in the acute forms as to mislead one in diagnosis.

The laboratory contributes little information. Leucocytosis is almost always detectable, and is usually high. Glycosuria, contrary to logical expectation, is usually absent. The great majority of tests have been directed towards the investigating of faeces for the possible presence of undigested material and the absence of ferments, of duodenal contents, and of urine for increased ferments. Loewe's adrenalin test for pupillary dilation might be tried. It is to be remembered, however, that most of these tests are applicable only in the less acute forms when the patient does not demand immediate operation.

Diagnosis.

The diagnosis of acute pancreatitis is difficult, and is more often than not recognized first at operation. Moynihan says the disease, however, should present little difficulty, as no other catastrophe within the abdomen produces such unendurable agony and collapse. Its frequent association with biliary disease both suggests and masks the diagnosis. The diseases from which acute pancreatitis must be differentiated are acute intestinal obstruction, perforation of a peptic ulcer, acute cholecystitis, acute appendicitis, and sometimes rupture of an ectopic pregnancy, mesenteric thrombosis and coronary thrombosis.

Treatment.

The treatment of acute pancreatic necrosis is essentially surgical. Operation should, as a rule, be performed immediately if the condition is acute and seen early. If, however, the case is one of so-called pancreatic apoplexy, or if the patient is seen first on the second or third day when a severe toxic general peritonitis has set in, operation might be delayed and general supportive measures adopted.

To be fair, one should state that not all surgeons practice immediate operation unless diffuse peritonitis or abscess formation supervene. Chief among whom are certain Danish[16] surgeons who report recovery in fifty consecutive cases treated either non-surgically or by delayed operation.

Those who practice immediate operation differ as to the type of procedure. Some favor a simple laparatomy with drainage to the general peritoneal cavity. Others make a direct attack upon the pancreas. Still others confine themselves to the gall bladder and its ducts. The method of choice, I feel, employs all the above procedures, adapting the operation to the peculiarities of the case.

The abdomen is opened by a right rectus incision, and any blood-stained peritoneal exudate is aspirated. The general abdominal cavity is explored, areas of fat necrosis being observed, and the pancreas is approched through the gastrohepatic or the gastrocolic omentum. The portions of the necrotic tissue which are free may be removed, but those which are attached should not be released because of the possibility of haemorrhage and the escape of pancreatic fluid. Some incise the capsule and open the gland by blunt dissection. Most experienced surgeons, however, are content to drain to but not into the gland.

At this stage of the operation the biliary tract is usually explored. In practically two-thirds of cases cholecystitis is present, and in over half cholelithiasis accompanies. If the patient is very acutely ill, and if the cystic duct is patent, cholecystostomy only for gallstones may be made. If, on the

may be performed, and a hurried search other hand, the patient's condition is fair, a cholecystectomy may be performed and a "T" tube placed in the common bile duct. This special attention to the biliary system seems justified for several reasons. First, the patients seem to do better; and, second, the etiology of the disease points emphatically to the biliary system.

Few surgical procedures are associated with as varied an assortment of inherent complications. Secondary hemorrhage occurs in 20% of cases and is due to the tryptic digestion of blood vessel walls.

Defective wound healing due to discharge of the pancreatic secretion accounts for two common sequelae, persistent sinus and ventral hernia.

A recurrent attack during convalescence or later may be a fatal event.

The syndrome of "pancreatic asthenia" with fall in blood pressure anorexia, nausea and loss of weight, may occur during convalescence and be helped by the administration of pancreatic extract.

Diabetes, strangely enough, is very rare, but if appearing can be treated successfully.

The mortality of all cases of acute pancreatic necrosis is close to 50%. This high incidence of death is due essentially to the collapse consequent to the profound toxaemia, or, as some say, to the stimulation of the solar plexis. There is no doubt, however, that untimely operative interference or injudicious temporizing along with numerous complications are contributing factors.

References.

1. Mann, F. C., and Giordano, A. S. The Bile Factor in Pancreatitis, Arch. Surg., 1923, 6, 1.
2. Opie, Eugene L. Disease of the Pancreas, 1910. Ed. 2.
3. Cameron and Noble—Quoted by Opie in Disease of Pancreas.
4. Maugeret, Reine, These de doct., Paris, 1908.
5. Franke, C., Relationship of Lymphatics of the Gall-bladder to the Pancreas, Deutsch. Ztschr. f. Chir. III: 539, 1911.
6. Bartels, P., Das Lymphgefassystem, in v. Bardeleben's Handbuch d. Anatomie des Menschen, Jena, 1909, Vol. 3.
7. Bernard, Calude, Memoirs sur Pancreas, 1856.
8. Flexner, imon, Jour. Exp. Med. 1906, VIII, 167.
9. Archibald, Edward, Surg. Gyn. and Obst., 1919 XXVIII, 529.
10. Polya, Mitt. a.d. Grenzgeb. d. Med. u. Chir. 1912, XXIV.
11. Archibald, Edward. See reference "9."
12. Opie. Eugene L., See reference "2."
13. Deaver, J. B., Pancreatitis, Surg. Clinics of N. America, 1921, Feb. 1.
14. Fitz, Reginald, Med. Record—1889, XXXV, 197.
15. Moynihan, Berkely, Ann. Surg., 1925, LXXXI, 132.
16. Mickelson, O., Hosp.—Tid., 1927, LXX, 1131.

THE CLINICAL SIGNIFICANCE OF HAEMATEMESIS

By M. SCOFFIELD, '33.

Haematemesis is the vomiting of blood from the stomach. When abundant, it is bright red and partly clotted, but some of it may be dark brown owing to partial digestion, and acid in reaction, with more or less food present. Blood from the lungs is always bright red, frothy and alkaline, usually having no clots. If the history of the patient and physical examination is insufficient, one should examine the stools for two or three days after, because haematemesis never occurs without some blood in the stools. However, confusion may arise due to the patient vomiting after an attack of haemoptysis.

Haematemesis does not always accompany haemorrhage of the gastro-intestinal tract, nor is it always evidence of disease in the upper part of the gastro intestinal tract. It occurs very infrequently in many diseases, and only in a few is it an expected, and an almost certain, incident. In the former groups, which, unfortunately for diagnosis, includes many diseases, it is of little significance from any point of view in the course of the disease. In the latter group — chiefly in certain conditions of the upper alimentary tract — it invariably has a bearing, either as a help in diagnosis and prognosis, or as an indication for treatment. The very fact, however, that it does occur, though very rarely, in many conditions, materially increases the difficulty in diagnosis in those cases where haematemesis is very common, and makes it necessary for us to be wary in dealing with many cases of bleeding from the stomach.

Reports in literature of the unusual case gives one a distorted view of the relative importance of the various causes of hematemesis.

Balfour divides cases into an Intragastric group, including ulcers, carcinomas, haemorrhagic lesions, and benign tumors; and an Extragastric group consisting of ulcer of duodenum, and diseases of liver, diseases of spleen, etc.

Miller in studying 151 cases lists these causes in order of frequency:

64% Peptic Ulcer (gastric and duodenal).
22% Gastric Carcinoma.
9% Splenic anaemia.
5% Cirrhosis of liver.
Other causes infrequent.

Rivers and Wilber reviewed 668 cases who cases to clinic in 1927 and 1928 with the complaint of Haematemesis. These writers group their cases into three classes:

(1) *Intrinsic gastro-duodenal or jejunal lesions.* 90% of the patients come in this group. Duodenal ulcer caused 50% of the haemorrhages; gastric ulcers caused 64%, which is important when one considers that this type of ulcer is relatively much less common than the duodenal ulcer. Carcinoma of the stomach accounted for fewer than 13% of the cases. Other causes, 0.9%, were: benign myoma of stomach, pyloric lesion, gastric syphilis with hepatic involvement, adenoma of duodenum and cholecystoduodenal fistula. In this group indigestion was characteristically present in the majority.

(2) *Haemorrhage in which varices seemed of significance,* the varices being gastric or oesophageal. Here were found 5% of the cases as follows:

1.8% cirrhosis of liver.
2.7% splenic anaemia.
0.6% cases resting between these two n which haemorrhage occurred after splenectomy. Indigestion was not so frequently present in this group.

(3) *Infrequent causes of haematemesis* — 4.5%.

1. 9% cholecystitis.
0. 3% Hemolytic Icterus.
0.15% Hemaphilia.
0.15% Haemorrhagic purpura.
2. 2% Indeterminate.

These figures show that vomiting of blood is a rare complication in blood dyscrasia. Usually in these cases the diagnosis is evident before the haematemesis occurs, but some times there are no previous symptoms, and on more than one occasion the abdomen has been opened unnecessarily.

Matthew of the Royal Infirmary, Edinburgh, found that of 2,600 cases admitted to the wards during a period of six years, 60 had the symptoms of haematemesis. Omitting the acute infections such as typhoid and others, which occasionally cause haematemesis, Matthew groups his cases into two:

(1) Haematemesis which occurs rarely in rather rare diseases: pernicious anaemia, splenic anaemia, lymphatic leukemia, polycythaemia vera, granular disease of the kidney, more rarely in haemophilia, purpura haemorrhagica, scurvy, acute appendicitis, more rarely still—acute yellow atrophy, malaria, etc.

(2) From the upper alimentary tract — stomach, duodenum, and liver.

55 of the 60 cases, i.e., 92%, occurred in the second group as follows:

18—gastric ulcer (acute and chronic).
15—duodenal ulcer.
15—gastric carcinoma.
2—alcoholic gastritis.
2—cirrhosis of liver.
3—spontaneous.

Five of the 60 cases occurred in group (1) as follows:

3—high blood pressure.
1—polycythaemia vera.
1—diabetic coma.

It will thus be seen that only a few stomach conditions ever have haematemesis, its occurrence being confined to gastric ulcer, gastric carcinoma, occasionally acute gastritis and cases of spontaneous haemorrhage. It is common also in duodenal ulcer.

Gastric Ulcer.

Of 40 cases of gastric ulcer, 18 had haematemesis, two being acute and 16 chronic gastric ulcer. Only five of the examples with chronic ulcer were men, the rest, acute and chronic, were in women. Thirteen were 30 years of age or under.

Acute gastric ulcer is not nearly so common as chronic ulcer, and occurs usually in young women under 30 years of age. The ulcer may be anywhere in the stomach — pylorus, body, or cardiac end in order of frequency. The haemorrhage is usually the first symptom, though some may have typical pain and vomiting for some little time before. The haematemesis is large, and usually of fresh blood. In the two cases mentioned this was so. There was no repetition of the haemorrhage and both patients, though weak and anaemic for a considerable time, made an uninterrupted recovery.

In most cases of chronic ulcer, the appearance of haematemesis settles the diagnosis. Typical chronic gastric ulcer patients have definite gastric symptoms — chiefly pain and vomiting — pain setting in about half an hour after food, situated in the epigastrium and increasing in severity, ultimately followed by vomiting of food, which relieves the pain. About half of the cases had such typical symptoms. But difficulties arose in the other cases. In them the symptoms were vague, irregular and intermittent. They had, over a period of years, attacks of so-called dyspepsia — fullness and distension after a meal, flatulence, usually some pain, varying in severity, and sometimes vomiting — the latter varying with the severity of the attack. Such attacks were present at longer or shorter intervals over a period of years, and finally, as in seven of the cases, during an attack haematemesis appears. The bleeding without doubt determines the presence of an ulcer.

The haemorrhage varies from a considerable quantity, though in no case so large as in the acute cases, to the vomiting of coffee-ground material. Sometimes, too, the bleeding is slight, and so slow that haematemesis does not occur, the blood passes into the bowel and is detected in the faeces.

When a chronic ulcer bleeds, the source of blood is generally a small vessel, most frequently an artery, which has become eroded. If death occurs as a result of haemorrhage, the artery involved is a branch of the coronary, the splenic or the gastro-epiploric artery in the case of the stomach, or the pancreatico-duodenal artery in the case of the duodenum. Such large haemorrhage may occur on the lesser curvature or posterior wall of the stomach, but usually only the posterior wall in the duodenum. Hurst points out the difficulty in obtaining an accurate percentage of haemorrhage in peptic ulcer because whereas few cases with gross haemorrhage fail to be diagnosed, many cases without haemorrhage remain classed as dyspepsia. Thus he estimates the true incidence of haemorrhage as about 10 per cent.

Haematemesis only occurs if the distension of the stomach caused by the haemorrhage is comparatively sudden, otherwise the walls relax as for a meal, and the stomach behaves as, after a meal of course, in carcinoma of the stomach; for example. the vomiting is due more to the presence of the growth itself than to the haemorrhage, which is usually small in quantity and occurs slowly.

Haemorrhage is an indication of activity of the ulcerative process. It never occurs whilst a patient is under strict medical treatment. Usually the pain has been aggravated for a few days preceding the haemorrhage, though the patient rarely vomits blood whilst he is actually suffering from pain. The pain passes off as the bleeding becomes more profuse owing to the relief of local congestion. For the same reason the pain rarely returns until several weeks later, even without rest and diet. Occasionally actual healing appears to take place.

Duodenal Ulcer.

In the Matthew series are 64 cases of duodenal ulcer, 15 of which had haematemesis, 58 of the 64 were in men, and almost all under 40 years of age. All 15 cases entered hospital because of haematemesis and not with a diagnosis of duodenal ulcer. The haemorrhage was severe in all 15 cases, and was repeated and very severe in six cases, four of whom died. The bleeding in these cases is by no means the first symptom the patient suffers from, but it is the one which forces him to seek advice. It is quite probable that everyone of the cases might have been recognized as duodenal ulcer before haematemesis appeared, though it is not always possible to anticipate haematemesis in duodenal ulcer.

When the patient is first seen during a severe haemorrhage, difficulties in diagnosis may arise, due to the fact that he is unable to give a proper history of his condition, and physical examination often does not give any positive information. However, the severity is always very suggestive.

Carcinoma Of Stomach.

Of 45 cases of gastric carcinoma, 15 had haematemesis, i.e., 33%. Incidentally, it is interesting to note that the cases of carcinoma of the stomach with haematemesis exceed in number the cases of gastric ulcer. Haematemesis in carcinoma of the stomach is not of special diagnostic significance, nor a really vital part in the disease. Nor is it often large in amount, more frequently it appears as coffee ground vomiting or occult blood in the vomit. The condition is almost always recognised from the other evidence before haematemesis appears. This was so in 13 of the cases with haematemesis. The other two were admitted following a brisk haemorrhage, and were cases of carcinoma in an advanced stage. In early

carcinoma, when the stomach symptoms are as yet vague and indefinite, the finding of occult blood in the vomit, especially on several occasions, is an important point in diagnosis. An increased frequency in vomiting with haematemesis, or increasing amount of vomited blood, indicate a more rapid progress of the growth in the stomach.

Gastritis.

Two cases of alcoholic gastritis had acute vomiting with haematemesis. It merely indicates a severely congested mucous membrane of the stomach.

Spontaneous Gastric Haemorrhage.

In these three cases, the diagnosis was uncertain, but a condition outside the stomach could be definitely excluded. The patients were women, between 30 and 40 years of age, and all were admitted to hospital with the history of a sudden large haematemesis of bright red blood. None of them looked ill on admission. Thorough examination was entirely negative, both subjectively and objectively. The haemorrhage did not recur in any of the cases, and a rapid recovery ensued. Similar cases have been operated upon, but no source of the haemorrhage could be found on opening the stomach. Many theories have been offered to account for these peculiar haemorrhages, but as yet the cause remains unknown.

Cirrhosis of the Liver.

Vomiting of blood, whether it is derived from the oesophagus or stomach, is a common symptom of cirrhosis of the liver. Indeed, it may be the initial symptom, though many go to an advanced stage and have jaundice or ascites or both and yet no haemorrhage. In either case like jaundice and ascites the haematemesis is a late phenomenon in the disease from the pathological point of view, and its appearance is a serious portent. The bleeding signifies a decided obstruction to the portal circulation, and may come from the veins of the stomach or from the rupture of a vein or veins at the lower end of the oesophagus which have become overdistended in an attempt to establish a free communication between the portal circulation and vena cava. There is not likely to be any difficulty in diagnosis. As a laboratory aid, one finds that the laevulose test always shows definite hepatic insufficiency, which has never been observed in peptic ulcer.

Conditions Outside the Alimentary Tract In Which Haematemesis Occurs.

Only three such conditions are discussed here, but a complete list is given by French.

High Blood Pressure: Patients with high blood pressure are common, but haematemesis must occur in very few. These patients are past middle life. The haemorrhage is excessive, of bright red blood, and comes on suddenly. The patient may be sent to hospital as gastric ulcer, and this is where confusion may arise. Post-mortem examination reveals no ulcer, and no actual source of the haemorrhage can be found. The smaller blood-vessels in the stomach and intestine, however, show arteriosclerosis and atheroma, but no actual bleeding point can be detected. The kidneys show the changes of interstitial nephritis. Like epistaxis, haematemesis in high blood pressure occurs in the later stages of the disease, and probably only in cases of high blood pressure associated with interstitial nephritis. The cause of the haemorrhage will always be revealed on examination by the hypertrophied left ventricle and estimations of urea output, etc. And the possibility of such a causation will have to be remembered in cases of sudden profuse haematemesis, which may also occur, as we have seen, in acute gastric ulcer, duodenal ulcer, and perhaps splenic anaemia.

Polycythemia Vera: In this uncommon condition, haematemesis may frequently occur, and with entirely beneficial results. The very high red count prevents error in diagnosis.

Splenic Anaemia: Sudden and profuse haemorrhage is one of the cardinal symptoms of splenic anaemia. However, physical examination of the patient reveals the marked enlargement of the spleen with secondary anaemia and leucopenia but no digestive symptoms, leaving no doubt as to the diagnosis. When this occurs the removal of the spleen is indicated.

Treatment Of Haemorrhage From Peptic Ulcer.

Hurst gives a concise outline: Complete immobility (a) of the patient keeps the blood pressure down; (b) of the stomach and duodenum prevents a newly-formed clot from being dislodged. An empty contracted stomach, like an empty contracted uterus, has no lumen, and its effect on haemorrhage is the same.

Morphia is given the patient subcutaneously to keep him quiet, and atropine to inhibit as much as possible the secretion of gastric juices. Complete starvation should be continued until no bleeding has occurred for 48 hours. The ordinary treatment of an ulcer is then begun. Fluids are given per rectum, interstitially and intravenously.

When the haemorrhage is severe and continues after haematemesis has occurred, one endeavours to empty the stomach and cause it to contract. A stomach tube is passed just beyond the cardia. The stomach is then emptied. It is washed out with four ounces of ice-cold water, and the lavage repeated over and over until the water which comes back is no longer blood-stained. Instead of water, 1 in 1,000 ferric chloride solution can be used, as its styptic action may help to arrest bleeding. When the last traces of fluid have been removed, a drachm of 1 in 1,000 adrenalin is poured into the stomach before withdrawing the tube.

Tribasic phosphate of magnesia one drachm is shaken up in a little water and given as soon as possible after the haemorrhage, and then every hour during the day and every two hours during the night unless the patient is asleep. This is continued until feeding is begun, when it is replaced by the usual method of giving alkalis. The tribasic phosphate of magnesia has half the neutralizing power of an equal weight of sodium bicarbonate, and it does not stimulate the secretion of gastric juice, nor produce any gas when it neutralizes the acid as does sodium bicarbonate.

The patient's blood should be grouped at once and a donor found who is available at all times. Transfusion with 500 c.c. should be carried out at once if the haemoglobin percentage falls to 40. The patient's condition is watched closely, especially pulse, blood pressure, and haemoglobin percentage, which are recorded at half-hour intervals. Iron can be given by mouth or subcutaneously.

Operation is very rarely called for with the immediate object of arresting the haemorrhage. The only indication in the acute stage is the persistence of severe haemorrhage whilst the patient is under medical treatment, especially if he is past middle life, has a chronic ulcer, and arteries so degenerated that they are unlikely to contract sufficiently for satisfactory plugging by thrombosis.

The question follows: Is operation indicated when the patient has recovered from his acute symptoms, to prevent recurrence of haemorrhage? Results of surgery to date show that the liability to haemorrhage is just as great after an operation has been performed for a peptic ulcer as after medical treatment, whether the patient has already had a haemorrhage or not.

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Bibliography.

1. Rivers and Wilbur: The Diagnostic Significance of Haematemesis. J. A. M. A. May, 1932.
2. Matthew: The Clinical Significance of Haematemesis — Oxford Medical Publications, Gastro-Intestinal Diseases, 1928.

RADIUM IN THE TREATMENT OF CARCINOMA OF THE CERVIX UTERI*

By R. C. DICKSON, '34.

A clear understanding of the therapeutic use of radium demands a knowledge of the physics of this interesting element. Brief mention of some of the properties of the rays derived from well screened radium is perhaps not out of order.

A. Physics.

For comparative purposes, 2 mm. of brass has been adopted as a standard of radium filters. Equivalent to it are 1.3 mm. of silver or lead, or 0.5 mm. of platinum or gold. Such a filter effectively blocks the less penetrating radium emanations. Thus all Alpha and Beta particles are stopped and also the "softer" Gamma radiations. Thus only the hard or more penetrating Gamma rays pass through. As the thickness of the filter is increased more and more Gamma rays are cut out, but at the same time the average penetrating power of those remaining is increased. Gamma rays are true electromagnetic waves and have wave-lengths of the order of .5 to .01A. They are similar to X-rays, but are of shorter wavelength than those produced in the ordinary Roentgen tube used in radiography.

Although the result of such screening is to reduce greatly the intensity of the emanations available for therapeutic use, it accomplishes two very useful things.

(a) It cuts out all the Alpha and Beta particles which would otherwise produce severe necrosis of the tissues nearest to them.

(b) The production of a beam of highly penetrating Gamma rays is important, especially when treating a large tumour or a deeply seated one. It makes possible a maximum effect in the depths of a tumour with minimal damage to superficial tissues.

Without further discussion of this phase of the subject, I must pass to a consideration of

B. Biophysics Of Radium.

Considerable work has been done on the effect of radium on normal body tissues, but a discussion of the results of such work is beyond the scope of this paper. Let us pass, therefore, to a brief consideration of the effect of radium on malignant neoplastic tissue.

Ewing's observations of the changes in neoplastic tissue exposed to radium are interesting and instructive. The fact that these observations were made on Cervical Carcinoma make them particularly applicable to this paper. Briefly, they are as follows:

First Week—A marked hyperemia and the beginning of exudation of lymphocytes and polymorphonuclear leucocytes was observed.

Second Week—The tumour cells appeared swollen and many exhibited hydropic degeneration. The nuclei of the tumour cells exhibited pyknosis. Fusion giant cells were formed.

Third Week—A marked decrease in the number of tumour cells was noticed. Some appeared to undergo autolysis and others to be fragmented by the activity of the cells of the exudate.

Fourth and Fifth Weeks—By this time, in a responsive case, only a few nuclear fragments and occasional giant cells remained.

Meanwhile the reaction of the stroma has continued. The exudation of lymphocytes and polymorphonuclear leu-

* A paper given before the Alpha Omega Alpha Honourary Medical Fraternity.

cocytes increased. Capillary buds were formed and a proliferation of fiboblasts took place. Granulation tissue eventually replaces the tumour, and the free surface is covered by epithelium.

Ewing emphasis the fact that a favourable result of radium treatment of carcinoma is dependent upon the regulation of the radium dosage so as to produce degeneration of the tumour cells and stimulation of the stroma. The importance of the stroma response is further indicated by the study of the effect of an overdose of radium. In such a case a simple necrosis of tumour cells takes place, but the stroma too is injured. Blood vessels are particularly susceptible, and swelling of the endothelium of the capillaries is followed by thrombosis. This produces premature contraction of the scar tissue with three important sequelae.

(a) Distortion.

(b) The possible production of a chronic ulcer which will not heal, due to lack of nutrition, and which will become the site of persistent infection.

(c) The isolation of nests of tumour cells which remain, and may result in recurrence at some future time.

Viewing the various histological changes as a whole, Ewing believes that the radium reaction is not duplicated under any other conditions, and indicates a specific and selective action of radium on neoplastic tissue.

Just how radium produces these effects is not known. However, certain facts regarding the susceptibility of various tumours are known. In general, cellular rapidly growing tumours, such as lymphosarcoma, are most susceptible. The more primitive cell types are more susceptible than more highly differentiated ones. Finally, those tumours which are abundantly supplied with stroma and blood vessels are as a rule less susceptible than those in which stroma and blood vessels are scanty.

These facts lead to a consideration of—

C. The Pathology of Carcinoma of the Cervix Uteri.

Incidence—Various observers place the incidence of carcinoma of the uterus between 30% and 40% of all carcinomas in the female. Of these 90%—97% originate in the cervix.

Etiology—Carcinoma of the cervix is more common in women who have born children than in nullipara. The forty-two patients treated at the Toronto General Hospital between 1929 and 1931 averaged four pregnancies. Moreover, none were nulliparous. The trauma to which the cervix is exposed at the time of delivery, with resulting lacerations and perhaps later the production of cervical erosions, seem to be an important factor in the production of malignancy. Suspicious heterotopia and hyperplasia may sometimes be observed in the epithelium of a cervical erosion. One observer saw carcinoma develop in a patient whom he had treated for five years for such an erosion.

Leukoplakia also seems to predispose of cancer of the cervix. In fact, in no case which came under observation before the actual development of malignancy has carcinoma been known to develop in an otherwise healthy cervix. Chronic endocervicitis or some such lesion indicating chronic irritation was always present.

Morbid Anatomy.

(1). *Gross*—Ewing recognizes three stages in the gross appearance of carcinoma of the cervix.

a. *Early cases seldom recognized clinically.* May appear as—
   1. A hard nodule in the cervical lips.
   2. A circumscribed indurated ulcel of lip or canal.
   3. More diffuse, low, papillary growths covering a portion of the lip or canal.

b. As usually observed clinically at a somewhat later stage, the lesion may appear as—
   1. Extensive induration and swelling of the cervix.

2. An excavated ulcer.
3. Extensive cauliflower growths covering much of the canal or portio.

c. Established and advanced cases may show—

1. Extensive infiltration of the tissues with resultant thickening of the cervix, vagina, uterine wall and parametrium.
2. Wide excavation of the cervix and vagina, with frequent involvement of rectum or bladder, and the resultant production of fistulae.
3. Wide superficial extension with fungating cauliflower masses filling a large portion of the vagina.

In all such advanced cases the parametrial and paracervical tissues are involved with resultant fixation of the uterus. Metastases to the hypogastric and external iliac glands are almost constant findings, and distant metastases may be formed.

The League of Nations Cancer Commission in 1929 classified Carcinoma of the Cervix as seen clinically into the following four groups:

Group 1.—Lesion limited to the cervix, no parametrial or paracervical involvement, free mobility of the uterus.

Group 2.—Vaginal wall invaded, slight parametrial and paracervical involvement, some mobility of the uterus.

Group 3.—Extensive parametrial and paracervical involvement, complete fixation of the uterus.

Group 4.—Direct invasion of surrounding viscera or distant metastases.

(2). *Microscopic*—Martzloff's observations at the Johns Hopkins Hospital are interesting. He recognizes three types of epidermoid carcinoma and an adenocarcinoma. The latter is made up of low columnar cells and presents the same morphology as adenocarcinoma elsewhere. This tumour arises from the lining of the cervical canal and constitutes only about 3% of cervical carcinomas.

The epidermoid types are as follows:

(a) Basal cell or fat spindle cell carcinoma is characterized by cords or islands of large, round or polyhedral cells showing many mitotic figures. No epithelial pearls are seen, while storms and blood vessels are scanty. This is the most malignant type of cervical carcimona.

(b) Transitional cell carcinoma falls between the preceding and the following types both in morphology and degree of malignancy. Mitosis is commonly seen, pearls are occasional findings.

(c) Squamous cell or spinal cell carcinoma is composed of cells of a more mature appearance. Pearl formation is frequently observed, while mitosis is less prominent. Stroma and blood vessels are more plentiful. It is the least malignant type of carcinoma of the cervix.

All the epidermoid types are radiosensitive with the malignant forms more so than the more mature tpyes. Adenocarcinoma is radio-resistant. In malignancy it falls between the squamous cell and transitional cell types.

D. Treatment.

Any discussion of the details of technique will not be attempted here, but will be left to those better qualified to do so. Some of the broader principles of technique will, however, be presented in the hope that further discussion, by those experienced in the therapeutic use of radium, will follow.

On looking over the literature, it is seen that broadly speaking all clinics using radium follow one of two types of treatment.

One group advocate the use of small quantities of radium applied for a long period of time. They base their method of treatment on the theory that radium has its maximum effect on cells undergoing mitosis. If the exposure is short, many cells will not be in this

phase. The treatment is therefore prolonged so as to expose more dividing cells to radiation. To do this the amount of radium used must be reduced in order to prevent overdosage.

Those who use large quantities of radium for a short time, argue that the theoretical value of the former method is overbalanced by the fact that this method of treatment exposed the patient to greater danger from trauma, infection, and the spread of metastases.

Heyman at the Radiumhemmet, Stockholm, gives three treatments. The second is given one week after the first, and the third two weeks after the second. He employs 105-112 mg. of Radium element heavily filtered with 3-4 mm. of lead. The delivery of the 2400 mgm. hrs. which constitute each treatment requires about 24 hours.

Ira A. Kaplan at the Bellevue Hospital, New York, uses a slight modification of the Rigand technique in use at the Curie Institute, Paris. He uses small quantities of heavily filtered radium applied over a long period of time. The whole treatment is given at one time.

Simpson of Chicago first delivers two massive doses of 50 minutes' duration and 2 days apart. In these treatments he employs 1000 mc. of radon placed in the vagina. A few days or weeks later the cervical canal, if previously obstructed by the growth, becomes patent. Then 600 mg. radon in a flexible lead tube 4 mm. in diameter, are placed in the canal without previous dilation of the cervix.

William P. Healy at the Memorial Hospital, New York, also uses large quantities of Radium for a short time. He employs 400-1000 ms. of radon to deliver a dose of 1000-3000 mgm. hours from the vagina. The treatment therefore requires about three hours. Two or three days later 3000 ms. hrs. are delivered from the cervical canal over a period of 24 hours.

Certain details of technique which are employed in various clinics are of debatable value. For instance, the dilation of the cervix, for the purpose of inserting radium tubes, results in a certain amount of trauma with consequent danger of infection and metastases. Simpson's treatment as described above, carefully avoids this. This factor becomes very important if the canal is obscured by the growth, and many operators do not insert radium in the canal until radiation from the vagina has cleared the way.

Again, the daily removal of applicators from vagina and cervical canal and the administration of a vaginal douche, the whole process being repeated in five or more successive days. is of doubtful value. Although aimed at the prevention of infection it would appear that the resultant trauma with the danger of spreading the growth. more than equals the disinfectant value of the procedure.

Another technique of questionable advisability is the implantation of radon seeds or radium needles in the cervical tissue. Again the danger of trauma and metastases is present.

Time forbids the discussion of the relative merits of radium element and radon, of the value of intra-abdominal implantation and cross-fire radiation, of the use of external radiation with deep X-rays or radium bomb and of the various combinations of radium and surgery. The remaining time must be devoted to a brief consideration of some outstanding results.

E. Results of Treatment.

Comparison of results in the field of treatment is very unsatisfactory. The different clinical classifications use in various localities, the different interpretations of the word "operable," the clinical material available at different clinics, the combination of various treatments (e.g., radium and surgery), the amount of follow up work done, and finally, the way in which the results are recorded, make

comparison unsatisfactory. Some results are as follows:

Heyman, at the Radiumhemmet-Stockholm

Of 790 cases of all groups, including 50 hopeless cases who received only palliative treatment, Heyman had 20.6% five year clinical cures.

Of a 188 operable cases, excluding (i.e., counting as dead from carcinoma) 6 cases on whom hysterectomy was subsequently performed, but who were still alive, he obtained 40.4% of five year cures.

In the inoperable and borderline group 16% five year cures were obtained in 549 cases.

Lacasagne, at the Radium Institute, Paris, published the following results of 350 cases:

Group 1. 38 cases. 42% five year cures.
Group 2. 132 cases. 28% five year cures.
Group 3. 149 cases. 10% five year cures.
Group 4. 31 cases. . . . . five year cures.
All Groups—350 cases. 20% five year cures.

Ward and Farrar at the Women's Free Hospital, N.Y.:

Primary Mortality—1.6%.

Five year clinical cures, all groups, 24.7%

Five year clinical cures, 65 cases, Groups 1 and 2, 57.1%.

Ward and Farrar, and Heyman specially emphasize the importance of follow up work. In both these clinics the patients are kept under monthly observation for five years They also stress the importance of pre-operative or rather pre-radiation treatment which consists of general constitutional treatment, and blood transfusion to those patients whose haemoglobin is under 50%.

The Department of Gynaecology at the Toronto General Hospital organized a follow up clinic in December, 1929. Their results for two years were as follows:

In all 42 cases were treated. Of these 19% were of Group 1, 31% Group 2, 45% Group 3, and 5% Group 4.

Of these 42 patients 22 were in satisfactory condition two years after treatment, 8 were in unsatisfactory condition and 12 were dead. While these results cannot at this early stage be compared with the others quoted above, yet they offer the hope that a gratifying number of five year clinical cures will be obtained.

Before concluding this paper I would like to refer briefly to the surgical aspect of the treatment of carcinoma of the cervix. In this field the work of Victor Bonney is probably the most outstanding. A consideration of his results with the Wertheim Hysterectomy shows that even now the radium treatment of carcinoma of the cervix is equal, if not superior, to surgery.

Bonney found that 63% of the cases which came under his care were operative. It may be said here that Bonney considers as "operable" many cases which even outstanding surgeons would not attempt to treat. Of the 63% of operable cases 36.5% survived for 5 years or more, following Wertheim Hysterectomy. Three hundred and fifty-one cures were so treated. Thus about 22% of the cases which Bonney saw were clinically cured by surgery—and this surgery at its best. Over this series of cases the immediate operative mortality was 17.1%. Further consideration reveals that in his first 100 cases Bonney's operative mortality was over 20%, while in his last 100 cases it was about 14%. The per centage of 5 year cures, however, fell off as the primary mortality was reduced. Thus it appears that Bonney with his years of experience has brought the surgical treatment of this lesion to its peak. Better results can hardly be expected, and any hope of improvement in the treatment of carcinoma of the cervix, in the light of our present knowledge of malignancy, appears to lie in improved radiological technique, and in earlier diagnosis.

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